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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
STITZEL, DAVID PAUL	

ART UNIT	PAPER NUMBER
1616	

DATE MAILED: 10/19/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/724,337	CHOWDHURY ET AL.	
	Examiner	Art Unit	
	David P. Stitzel, Esq.	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 November 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-24* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

OFFICIAL ACTION

Status of Claims

Claims 1-24 are currently pending and therefore examined herein on the merits for patentability.

Claim Rejections - 35 U.S.C. § 102

The following is a quotation of the appropriate paragraph of 35 U.S.C. § 102, which forms the basis of the anticipation rejections as set forth under this particular section of the Official Action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-8, 10, 12-19 and 22-23 are rejected under 35 U.S.C. § 102(b) as being anticipated by U.S. Patent 6,294,192 (hereinafter the Patel '192 patent).

Claims 1-8, 10, 12-19 and 22 of the instant application are directed to an injectable pharmaceutical composition comprising tetrahydrocannabinol, an amphiphilic surfactant, an antioxidant, an oil, a salt, ethanol and water. Tetrahydrocannabinol is present in the amount of less than or equal to about 0.35% by weight. The amphiphilic surfactant is selected from the group consisting of Cremophor EL, Polysorbate 80, Poloxamer 407, Poloxamer 237, PEG 400, Pharmasolve, propylene glycol and hydroxypropyl cyclodextrin, which are present in the amount of less than or equal to about 20%, 15%, 2.5%, 5%, 20%, 10%, 60% and 30% by weight, respectively. The oil is corn oil, which is present in the amount of less than or equal to about

10% by weight. Ethanol is present in the amount of less than or equal to about 15% by weight. Water is present in the amount of less than or equal to about 90% by weight.

Claim 23 of the instant application is directed to a method of making a pharmaceutical composition comprising tetrahydrocannabinol, an amphiphilic surfactant, ethanol and water, wherein said method comprises: mixing tetrahydrocannabinol and ethanol to form a first mixture; mixing an amphiphilic surfactant and water to form a second mixture; and mixing said first mixture and said second mixture to form said pharmaceutical composition, which is either an intermediate or a final product.

Similar to claims 1-8, 10, 12-19 and 22 of the instant application, the Patel '192 patent discloses an injectable pharmaceutical composition (abstract; column 26, line 50) comprising tetrahydrocannabinol (column 22, line 15; column 24, line 65), an amphiphilic surfactant (column 5, lines 13-16), an antioxidant (column 26, line 18), an oil (column 8, lines 61-63), a salt in the form of an isotonic aqueous HEPES buffer solution (column 32, lines 10-11; and column 46, lines 28-29), ethanol (column 25, lines 20, 59 and 62) and water (column 25, line 51; and column 32, lines 9-10). Tetrahydrocannabinol is present in the amount of less than or equal to about 1% by weight and typically less than about 0.1% by weight (column 21, lines 47-57; column 22, line 15; column 24, line 65). The amphiphilic surfactant (column 5, lines 13-16) is selected from the group consisting of Cremophor EL (a.k.a., PEG-35 castor oil) (Table 5, column 10, line 25); Polysorbate 80 (Table 19, column 33 and 34, lines 7-9), Poloxamer 407 (column 16, lines 49-50; and Table 15, column 17, line 30); Poloxamer 237 (Table 15, column 17, line 30); and PEG 400 (Table 1, column 6, lines 43 and 46-47, and column 7, line 37); which are present in the amount from about 1% to about 60% by weight (column 21, lines 30-31); as well as

Pharmasolve (a.k.a., N-methylpyrrolidone) (column 25, line 57); propylene glycol (column 25, lines 21-22 and 63) and hydroxypropyl cyclodextrin (column 25, lines 26-27 and 59); which are present in the amount from about 1% to about 100% by weight (column 26, lines 12-13). The oil is corn oil, which is present in the amount from about 1% to about 60% by weight (column 8, lines 58-63; and column 21, lines 30-31). Ethanol is present in the amount from about 1% to about 100% by weight, including 50%, 25%, 10% and 5% by weight (column 25, lines 20, 59 and 62; and column 26, lines 8-14). Water is present in the amount from about 1% to about 100% by weight, including 50%, 25%, 10% and 5% by weight (column 25, line 51; and column 26, lines 12-13). It should also be noted that although the Patel '192 patent characterizes Pharmasolve (a.k.a., N-methylpyrrolidone) (column 25, line 57); propylene glycol (column 25, lines 21-22 and 63); hydroxypropyl cyclodextrin (column 25, lines 26-27 and 59); and ethanol as "solubilizers," the Patel '192 patent also discloses that "mixtures of solubilizers are also within the scope of the invention" (column 25, lines 52-53).

Similar to claim 23 of the instant application, the Patel '192 patent discloses a method of making a pharmaceutical composition comprising tetrahydrocannabinol, ethanol, an amphiphilic surfactant and water, as well as an optional additional additive, such as an antioxidant, wherein said method comprises: mixing a hydrophobic therapeutic agent, namely tetrahydrocannabinol, and a solubilizer, namely ethanol, to form a pre-concentrate; mixing an amphiphilic surfactant and water to form an aqueous carrier system; mixing said pre-concentrate and said aqueous carrier system to form an aqueous dispersion of said pharmaceutical composition; and optionally mixing an additional additive, such as an antioxidant, to said aqueous dispersion of said pharmaceutical composition (abstract; column 22, line 15; column 24, line 65; column 25, lines

15-20; column 26, lines 15-20, 25-28, and 61-67; column 27, lines 1-10; and column 28, lines 6-10).

Claim Rejections - 35 U.S.C. § 103

The following is a quotation of the appropriate paragraph of 35 U.S.C. § 103, which forms the basis of the obviousness rejections as set forth under this particular section of the Official Action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-22 of the instant application are directed to an injectable pharmaceutical composition comprising tetrahydrocannabinol, an amphiphilic surfactant, an antioxidant, an oil, a salt, ethanol and water. Tetrahydrocannabinol is present in the amount of less than or equal to about 0.35% by weight. The amphiphilic surfactant is selected from the group consisting of Cremophor EL, Polysorbate 80, Poloxamer 407, Poloxamer 237, PEG 400, Pharmasolve, propylene glycol and hydroxypropyl cyclodextrin, which are present in the amount of less than or equal to about 20%, 15%, 2.5%, 5%, 20%, 10%, 60% and 30% by weight, respectively. The antioxidant is sodium metabisulfite or ascorbyl palmitate. The oil is corn oil, which is present in the amount of less than or equal to about 10% by weight. The salt is sodium hydroxide or sodium chloride, which renders said pharmaceutical composition essentially isotonic and said sodium chloride is present in the amount of about 0.9% by weight. Ethanol is present in the

amount of less than or equal to about 15% by weight. Water is present in the amount of less than or equal to about 90% by weight.

Claim 23 of the instant application is directed to a method of making a pharmaceutical composition comprising tetrahydrocannabinol, an amphiphilic surfactant, ethanol and water, wherein said method comprises: mixing tetrahydrocannabinol and ethanol to form a first mixture; mixing an amphiphilic surfactant and water to form a second mixture; and mixing said first mixture and said second mixture to form said pharmaceutical composition, which is either an intermediate or a final product.

Claim 24 of the instant application is directed to a method of treating emesis, anorexia or wasting syndrome comprising injecting a therapeutically effective amount of a pharmaceutical composition comprising tetrahydrocannabinol, an amphiphilic surfactant, an antioxidant, an oil, a salt, ethanol and water.

1. Claims 1-23 are rejected under 35 U.S.C. § 103(a) as being unpatentable over the primary reference, namely the Patel '192 patent, in view of the secondary references, namely U.S. Patent Application Number 2002/0173549 (hereinafter the Wurtman '549 application); U.S. Patent Number 4,912,208 (hereinafter the Fiechtner '208 patent); and U.S. Patent Number 5,876,742 (hereinafter the Cochrum '742 patent). It should be noted however that the secondary references of the Fiechtner '208 patent and the Cochrum '742 patent are merely cited herein as pertaining only to claims 9, 20 and 21, and are solely relied upon to simply illustrate the state of the art with respect to isotonic aqueous HEPES buffer solutions containing sodium chloride in an amount of about 0.9% by weight.

Similar to claims 1-8, 10, 12-19 and 22 of the instant application, the Patel '192 patent discloses an injectable pharmaceutical composition (abstract; column 26, line 50) comprising tetrahydrocannabinol (column 22, line 15; column 24, line 65), an amphiphilic surfactant (column 5, lines 13-16), an antioxidant (column 26, line 18), an oil (column 8, lines 61-63), a salt in the form of a an isotonic aqueous HEPES buffer solution (column 32, lines 10-11; and column 46, lines 28-29), ethanol (column 25, lines 20, 59 and 62) and water (column 25, line 51; and column 32, lines 9-10). Tetrahydrocannabinol is present in the amount of less than or equal to about 1% by weight and typically less than about 0.1% by weight (column 21, lines 47-57; column 22, line 15; column 24, line 65). The amphiphilic surfactant (column 5, lines 13-16) is selected from the group consisting of Cremophor EL (a.k.a., PEG-35 castor oil) (Table 5, column 10, line 25); Polysorbate 80 (Table 19, column 33 and 34, lines 7-9), Poloxamer 407 (column 16, lines 49-50; and Table 15, column 17, line 30); Poloxamer 237 (Table 15, column 17, line 30); and PEG 400 (Table 1, column 6, lines 43 and 46-47, and column 7, line 37); which are present in the amount from about 1% to about 60% by weight (column 21, lines 30-31); as well as Pharmasolve (a.k.a., N-methylpyrrolidone) (column 25, line 57); propylene glycol (column 25, lines 21-22 and 63) and hydroxypropyl cyclodextrin (column 25, lines 26-27 and 59); which are present in the amount from about 1% to about 100% by weight (column 26, lines 12-13). The oil is corn oil, which is present in the amount from about 1% to about 60% by weight (column 8, lines 58-63; and column 21, lines 30-31). The salt is in the form of an isotonic aqueous HEPES buffer solution (column 32, lines 10-11; and column 46, lines 28-29). Ethanol is present in the amount from about 1% to about 100% by weight, including 50%, 25%, 10% and 5% by weight (column 25, lines 20, 59 and 62; and column 26, lines 8-14). Water is present in the amount

from about 1% to about 100% by weight, including 50%, 25%, 10% and 5% by weight (column 25, line 51; and column 26, lines 12-13).

With respect to claim 11 of the instant application, although the Patel '192 patent does not specifically mention utilizing sodium metabisulfite or ascorbyl palmitate as said antioxidant, the Patel '192 patent does teach a pharmaceutical composition comprising tetrahydrocannabinol and an antioxidant (column 22, line 15; column 24, line 65; column 26, line 18). One of ordinary skill in the art would readily envision sodium metabisulfite and ascorbyl palmitate as being within the scope of the Patel '192 patent, as said antioxidants are commonly known in the art. Notwithstanding the aforementioned rationale regarding the obviousness associated with utilizing sodium metabisulfite and ascorbyl palmitate as said antioxidant, it would have been obvious to one of ordinary skill in the art to incorporate the sodium metabisulfite and ascorbyl palmitate antioxidants taught in the Wurtman '549 application, as the antioxidant taught in the Patel '192 patent. Sufficient motivation, as well as a reasonable expectation of success, exists as the Wurtman '549 application teaches incorporating said sodium metabisulfite and ascorbyl palmitate antioxidants ([0074]) into a pharmaceutical composition comprising cannabinoids ([0012] and [0037]).

With respect to claims 9 and 20-21 of the instant application, although the Patel '192 patent teaches a pharmaceutical composition comprising a salt, which is in the form of a isotonic aqueous HEPES buffer solution that renders said pharmaceutical composition essentially isotonic (column 32, lines 10-11; and column 46, lines 28-29), the Patel '192 patent does not specifically mention utilizing sodium hydroxide or sodium chloride as said salt, wherein said sodium chloride is present in the amount of about 0.9% by weight thereby rendering said pharmaceutical

composition essentially isotonic. Despite the aforementioned, the Patel '192 patent does teach incorporating an isotonic aqueous HEPES buffer solution into said pharmaceutical composition (column 32, lines 10-11; and column 46, lines 28-29). An isotonic aqueous HEPES buffer solution containing sodium hydroxide and sodium chloride, wherein said sodium chloride is present in the amount of about 0.9% by weight, is very well-known in the art. See e.g., the Fiechtner '208 patent (column 19, lines 61-63); and the Cochrum '742 patent (column 7, lines 22-24). Sodium chloride present in an amount of about 0.9% by weight is defined by the Applicants in claims 20 and 21 of the instant application as rendering said pharmaceutical composition essentially isotonic. Therefore, one of ordinary skill in the art would readily envision that the isotonic aqueous HEPES buffer solution taught in the Patel '192 patent, which comprises sodium chloride in an amount of about 0.9% by weight, would also render said pharmaceutical composition essentially isotonic.

Similar to claim 23 of the instant application, the Patel '192 patent discloses a method of making a pharmaceutical composition comprising tetrahydrocannabinol, ethanol, an amphiphilic surfactant and water, as well as an optional additional additive, such as an antioxidant, wherein said method comprises: mixing a hydrophobic therapeutic agent, namely tetrahydrocannabinol, and a solubilizer, namely ethanol, to form a pre-concentrate; mixing an amphiphilic surfactant and water to form an aqueous carrier system; mixing said pre-concentrate and said aqueous carrier system to form an aqueous dispersion of said pharmaceutical composition; and optionally mixing an additional additive, such as an antioxidant, to said aqueous dispersion of said pharmaceutical composition (abstract; column 22, line 15; column 24, line 65; column 25, lines

15-20; column 26, lines 15-20, 25-28, and 61-67; column 27, lines 1-10; and column 28, lines 6-10).

Therefore, the claimed invention, as a whole, would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made, because each and every element of the claimed invention, as a whole, would have been reasonably disclosed or suggested by the teachings of the cited prior art references.

2. Claims 1-8, 10, 12-19 and 22-24 are rejected under 35 U.S.C. § 103(a) as being unpatentable over the primary reference, namely the Patel '192 patent, in view of the secondary reference, namely U.S. Patent 5,804,592 (hereinafter the Volicer '592 patent).

Similar to claims 1-8, 10, 12-19 and 22 of the instant application, the Patel '192 patent discloses an injectable pharmaceutical composition (abstract; column 26, line 50) comprising tetrahydrocannabinol (column 22, line 15; column 24, line 65), an amphiphilic surfactant (column 5, lines 13-16), an antioxidant (column 26, line 18), an oil (column 8, lines 61-63), a salt in the form of an isotonic aqueous HEPES buffer solution (column 32, lines 10-11; and column 46, lines 28-29), ethanol (column 25, lines 20, 59 and 62) and water (column 25, line 51; and column 32, lines 9-10). Tetrahydrocannabinol is present in the amount of less than or equal to about 1% by weight and typically less than about 0.1% by weight (column 21, lines 47-57; column 22, line 15; column 24, line 65). The amphiphilic surfactant (column 5, lines 13-16) is selected from the group consisting of Cremophor EL (a.k.a., PEG-35 castor oil) (Table 5, column 10, line 25); Polysorbate 80 (Table 19, column 33 and 34, lines 7-9), Poloxamer 407 (column 16, lines 49-50; and Table 15, column 17, line 30); Poloxamer 237 (Table 15, column 17, line 30);

and PEG 400 (Table 1, column 6, lines 43 and 46-47, and column 7, line 37); which are present in the amount from about 1% to about 60% by weight (column 21, lines 30-31); as well as Pharmasolve (a.k.a., N-methylpyrrolidone) (column 25, line 57); propylene glycol (column 25, lines 21-22 and 63) and hydroxypropyl cyclodextrin (column 25, lines 26-27 and 59); which are present in the amount from about 1% to about 100% by weight (column 26, lines 12-13). The oil is corn oil, which is present in the amount from about 1% to about 60% by weight (column 8, lines 58-63; and column 21, lines 30-31). Ethanol is present in the amount from about 1% to about 100% by weight, including 50%, 25%, 10% and 5% by weight (column 25, lines 20, 59 and 62; and column 26, lines 8-14). Water is present in the amount from about 1% to about 100% by weight, including 50%, 25%, 10% and 5% by weight (column 25, line 51; and column 26, lines 12-13).

Similar to claim 23 of the instant application, the Patel '192 patent discloses a method of making a pharmaceutical composition comprising tetrahydrocannabinol, ethanol, an amphiphilic surfactant and water, as well as an optional additional additive, such as an antioxidant, wherein said method comprises: mixing a hydrophobic therapeutic agent, namely tetrahydrocannabinol, and a solubilizer, namely ethanol, to form a pre-concentrate; mixing an amphiphilic surfactant and water to form an aqueous carrier system; mixing said pre-concentrate and said aqueous carrier system to form an aqueous dispersion of said pharmaceutical composition; and optionally mixing an additional additive, such as an antioxidant, to said aqueous dispersion of said pharmaceutical composition (abstract; column 22, line 15; column 24, line 65; column 25, lines 15-20; column 26, lines 15-20, 25-28, and 61-67; column 27, lines 1-10; and column 28, lines 6-10).

With respect to claim 24 of the instant application, although the Patel '192 patent teaches administering an injectable tetrahydrocannabinol pharmaceutical composition parenterally (column 26, line 50), the Patel '192 patent does not specifically mention a method of treating emesis, anorexia or wasting syndrome. However, it would have been obvious to one of ordinary skill in the art to parenterally administer the injectable tetrahydrocannabinol pharmaceutical composition taught by the Patel '192 patent (column 22, line 15; column 24, line 65; and column 26, line 50) to treat emesis, anorexia and wasting syndrome, as the Volicer '592 patent teaches the parenteral (i.e., intravenous, intramuscular or subcutaneous) administration of an injectable pharmaceutical composition comprising dronabinol (a.k.a., Marinol®), which is a synthetic Δ^9-tetrahydrocannabinol, to treat emesis (i.e., nausea and vomiting), anorexia and wasting syndrome (column 2, lines 5-11 and 39-46). Sufficient motivation, as well as a reasonable expectation of success, exists as the Volicer '592 teaches administering a parenterally injectable pharmaceutical composition comprising a synthetic Δ^9-tetrahydrocannabinol for treating various pathological conditions, while the Patel '192 patent likewise teaches administering a parenterally injectable pharmaceutical composition comprising naturally occurring tetrahydrocannabinol for treating various pathological conditions.

Therefore, the claimed invention, as a whole, would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made, because each and every element of the claimed invention, as a whole, would have been reasonably disclosed or suggested by the teachings of the cited prior art references.

Conclusion

Claims 1-24 are rejected.

Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David P. Stitzel, Esq. whose telephone number is 571-272-8508. The examiner can normally be reached on Monday-Friday, from 7:00AM-5:30PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary L. Kunz can be reached at 571-272-0887. The central fax number for the USPTO is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published patent applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished patent applications is only available through Private PAIR. For more information about the PAIR system, please see http://pair-direct.uspto.gov. Should you have questions about acquiring access to the Private PAIR system, please contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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